Applicant: ChangSheng Liu et al. Attorney's Docket No.: 16969-017001

Serial No.: 09/676,526 Filed: October 2, 2000

Page : 2 of 13

Amendments to the Specification:

Please replace the Title with the following Title:

METHOD FOR IN-SITU CALIBRATION OF ELECTROPHORETIC ANALYSIS SYSTEMS.

Please replace the paragraph beginning with "The principle" at page 2, line 9, and ending with "relationship:" with the following amended paragraph:

The principle behind the calibration coefficients is that a spectrum of received light intensities in each of the channels is caused by the spectrum of a single dye (tagging a corresponding base) weighted by the effects (calibration coefficients) of the detection system. If $I_0(n)$, $I_1(n)$, ..., $I_9(n)$ represent the measured intensities of the R = 10 channels at the nth set of outputs from the CCD (after preprocessing including detection, binning and baseline subtraction), $B_0(n)$, $B_1(n)$, ..., $B_3(n)$ is a vector representing the contribution (presence 1 or absence 0) from of the M = 4 bases, and C_{ij} are coefficients of a known 10 x 4 matrix which maps the bases onto the detected channels, we then having have the following relationship:

Please replace the paragraph beginning at page 5, line 20, with the following amended paragraph:

Figs. 13a-13b <u>13a-13d</u> present calibration coefficient matrices for each of four dye sets commonly used in DNA sequencing;

Please replace the paragraph beginning at page 5, line 25, with the following amended paragraph:

Fig. 17 Figs. 17a-17g shows typical morphologies seen in contoured time-frequency plots, such as those shown in Figs. 14-16.

Please replace the paragraph beginning at page 8, line 8, with the following amended paragraph:

Applicant: ChangSheng Liu et al. Attorney's Docket No.: 16969-017001

Serial No.: 09/676,526 Filed : October 2, 2000 Page : 3 of 13

(4) Peak assembly. This is a process to remove a peak happens that occurs only in one channel (i.e., a peak that is not physically sound) and to identify as same peak if determine whether a the peak maximum is shift has been shifted one frame due due to mathematical manipulation, and then determine the proper band location in the time domain. Most of the peak maximums in more than one channel happen at a specific time. At least two channels have shown peaks at a specific time. Since the individual channel has been carried out baseline subtraction separately. Sometimes peak maximum maxima may shift a frame in the time domain. It is the same peak even if the peak position is shifted a frame in different color channels. Peak intensities in all of the channels are summed in the time domain. shown in Figure b.

Please replace the paragraph beginning at page 8, line 16, with the following amended paragraph:

Fig. 3 depicts a portion of the raw time series intensity data Xi, i representing the time index of the sample, for each of the 10 channels from a single capillary during a DNA sequencing run. At any given instant, only a few channels exhibit a peak because each of the four dyes only has a finite bandwidth. The raw data intensity signals Xi from each of the 10 channels, for each capillary, are stored for future processing to create the multicomponent matrix and also to identify the fluorescent species giving rise to the detected fluorescent intensities. The pick-picking peak-picking process is carried out through all of the 10 traces to give the peak position in time domain. A peak due to the specific type of molecules in the sample will show up at a specific time in more than a trace because of the spectra overlapping. For example in Fig. 3, a peak at 52 min has shown up in trace 3 to trace 9. The peak-picking program will pick up the peak from trace 3 to trace 9. A peak at 51.9, just prior to the peak at 5000, has shown up from the trace 0 to trace 6. At the specific time that a peak shows up in more than one channel, the peak intensities for all 10 channels are recorded for the data processing step. The channel number of maximum intensity over all of the ten channels is also recorded at the specific time.

Applicant: ChangSheng Liu et al. Attorney's Docket No.: 16969-017001

Serial No.: 09/676,526 Filed: October 2, 2000

Page : 4 of 13

Please replace the paragraph beginning at page 9, line 8, with the following amended paragraph:

(b) Identifying the overlapped peaks by peak-fitting software. After these peaks are identified, peak widths can be identified with a peak-fitting software. In most electrophoresis separation separations, the peaks coming out at the first section of the electropherograms electropherogram are usually very sharp and the peaks in the late section of separation usually wide. However, the peak widths in a small local section, for example, in 300 frames, are practically the same. This concept is very important to resolve the temporal overlapping peaks in a local section. In DNA analysis, the complete overlapping bands with different DNA size in time domain are rare. Most of the overlap is confined to the rising or tailing edge of the peaks where one enters into the detection window and the other is moving out the windows. The overlapping peaks often are 30% wider than single peak in DNA separation. If intensity of a peak in a channel is small, 20% of local maximum intensity, we did not calculate the peak width due to its low intensity. The peak width and spacing at a specific moment can calculate from the ten traces of the data.

Please replace the paragraph beginning at page 16, line 27, with the following amended paragraph:

(4) Additional peak rejection. If the difference between any one of the 10 normalized coefficients for a peak within a particular group (G, A, T or C) and the group average for that coefficient is bigger than a predetermined times (e.g., 1.5 times) the group standard deviation for that coefficient, that peak is rejected and not used in coefficient calculations.